

REMARKS

As an initial matter, Applicants wish to thank the Examiner for the courtesy of the telephonic interview conducted on July 5, 2007. A summary of the telephonic interview is attached hereto as Exhibit A.

Claims 1 to 20 are currently pending in the application. All of the claims were rejected. By this amendment, Applicants have amended claims 1, 16 and 19 and canceled claims 12 to 15 without prejudice. All of the amendments find full support in the specification and drawings as filed. No new matter has been added. In view of the above amendments and following remarks, Applicants respectfully submit that this application is in condition for allowance. Accordingly, reconsideration and a timely notice of allowance are respectfully requested.

Claim Amendments

Claims 1 and 19 have been amended to change “comprising” to “consisting essentially of”. Applicants respectfully submit that full support for this change is found in the specification and drawings as filed, for example on page 15, lines 9 to 26 of the specification and in Fig. 13. Claim 16 has been amended for clarity.

No new matter has been added. Applicants respectfully request entry of the above claim amendments.

Rejection Under 35 U.S.C. §112

The Examiner rejected claim 13 under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Although Applicants do not agree, Applicants have canceled claim 13 without prejudice in the interest of advancing prosecution. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Claim Rejections Under 35 U.S.C. §101

The Examiner rejected claims 16 to 18 pursuant to 35 U.S.C. §101 as being directed to non-statutory subject matter. Applicants respectfully traverse this rejection.

In the telephonic interview with the Examiner conducted on July 5, 2007, the Examiner indicated that he had reconsidered the propriety of this rejection and that he would withdraw the rejection in the next Office communication. Accordingly, Applicants do not address this rejection again here, except to incorporate the arguments made in the previous Response to Office action filed on January 22, 2007 by reference herein in their entirety.

Applicants respectfully request that this rejection be withdrawn.

Claim Rejections Under 35 USC §103

The Examiner rejected claims 1 to 3, 7 to 13 and 19 under 35 U.S.C. §103(a) as being unpatentable over Martin et al. (U.S. Patent No. 4,573,796) in view of Hansen et al. (U.S. Patent No. 4,284,412). Applicants have canceled claims 12 and 13 without prejudice, but address this rejection as to the remaining claims. In view of the amendments to claims 1 and 19, Applicants respectfully traverse this rejection. Applicants respectfully submit that Martin et al. and Hansen et al. fail to teach or suggest a system consisting essentially of “a plurality of triggers, each of the plurality of triggers being connected to a separate one of the plurality of scatter detectors” as recited in claims 1 and 19.

The present invention is directed to a system for measuring the irradiance of a fluorescently labeled particle. The system has a plurality of scatter detectors, each configured to detect light from only one of the plurality of excitation light sources; and a plurality of triggers, each trigger being independently connected to a separate scatter detector. Because there is a separate scatter detector and trigger corresponding to each excitation light source, and because the fluorescence detectors are configured to respond only to a discrete number of wavelength bands, precise alignment and spacing of the excitation light sources is not necessary. Accordingly, the system can accommodate excitation light source or core velocity drift.

Compared to the prior art, the system of the present invention has an increased range over which the lasers can be aligned to obtain good fluorescence information. It is not necessary to precisely align all of the excitation light sources to focus on the same point in the flow chamber or to have a precise spacing along the flow path.

Martin is directed to an apparatus for eliminating background interference during fluorescence measurements in a multiple laser flow cytometer by modulating one or more excitation light sources depending on the position of a particle. As seen from col. 4, line 46 to col. 5, line 8 and Fig. 1 of Martin et al., the triggers (Gate Signal Gen 1 (37) and Gate Signal Gen 2 (38)) are linked together, thereby linking each trigger to both scatter detectors. Therefore, each trigger is not coupled to a separate corresponding one of the plurality of scatter detectors as claimed.

The interconnected triggers have disadvantages. In contrast to the presently claimed invention, the apparatus of Martin requires preexisting knowledge of the separation between excitation light sources, and therefore cannot accommodate excitation light source or core velocity drift during the course of an experiment. As explained in col. 4, lines 60 to 63, “the first gate signal is, effectively, delayed for a time sufficient for first biological particle 20 to travel the distance S from the first light beam 18 to the second light beam 50.” As seen in col. 4, line 35 to col. 5, line 10, a delay system relying on the known distance between excitation light sources, coupled to first and second modulators and gate signal generators to control the integrators is key to achieving the object of the invention. The integrators are controlled by multiple triggers in response to light incident on multiple scatter detectors, thereby requiring precise alignment. Thus, Martin et al. fail to teach or suggest “a plurality of triggers, each of the plurality of triggers being connected to a separate one of the plurality of scatter detectors” as claimed.

Hansen et al. teach a flow cytofluorometric apparatus for processing blood. As seen in Fig. 1 and col. 4, lines 32 to 44, two lasers are precisely oriented to focus on the same point in the flow chamber. As seen in col. 4, lines 49 to 54, scatter from both lasers incident on three different scatter detectors are used to control integration. Applicants respectfully submit that Hansen et al. fail to remedy the defects of Martin et al. Therefore, Applicants respectfully

submit that claims 1 and 19 are patentable over Martin et al. and Hansen et al., either alone or in combination.

Claims 2, 3 and 7 to 11 depend from claim 1 and by definition contain all of the limitations of claim 1. Therefore, Applicants respectfully submit that claims 2, 3 and 7 to 11 are patentable over Martin et al. and Hansen et al. for the reasons given above regarding claim 1 as well as because of the additional limitations contained therein.

Accordingly, Applicants respectfully request that the rejection of remaining claims 1 to 3, 7 to 11 and 19 under 35 U.S.C. §103(a) be withdrawn.

The Examiner rejected claims 4 and 6 under 35 U.S.C. §103(a) as being unpatentable over Martin et al. (U.S. Patent No. 4,573,796) in view of Hansen et al. (U.S. Patent No. 4,284,412) and further in view of Pinkel (U.S. Patent No. 4,988,619). Applicants respectfully traverse this rejection.

Claims 4 and 6 depend from claim 1 and by definition contain all of the limitations of claim 1. As explained above with regard to claim 1, Martin et al. and Hansen et al., taken alone or in combination, fail to teach a system consisting essentially of: “a plurality of triggers, each of the plurality of triggers being coupled to a separate corresponding one of the plurality of scatter detectors.”

Pinkel is directed to a flow cytometry apparatus with an obstruction across the flow chamber to create a one dimensional convergence of a sheath fluid to orient flat cells. As seen in Fig. 1, and col. 2, lines 31 to 44, Pinkel only teaches the use of a single laser and does not teach a plurality of triggers or scatter detectors. Additionally, Applicants respectfully submit that one skilled in the art would have no motivation to combine Pinkel with the multi-laser systems of either Martin et al. or Hansen et al.

Therefore, Applicants respectfully request that the rejection of claims 4 and 6 under 35 U.S.C. §103(a) be withdrawn.

The Examiner rejected claim 5 under 35 U.S.C. §103(a) as being unpatentable over Martin et al. (U.S. Patent No. 4,573,796) in view of Hansen et al. (U.S. Patent No. 4,284,412) in further view of Kramer (U.S. Patent No. 6,743,634). Applicants respectfully traverse this rejection.

Claim 5 depends from claim 1 and by definition contain all of the limitations of claim 1. As explained above with regard to claim 1, Martin et al. and Hansen et al., taken alone or in combination, fail to teach a system “a plurality of triggers, each of the plurality of triggers being coupled to a separate corresponding one of the plurality of scatter detectors.”

Kramer is directed to a method and apparatus for differentiating blood cells using back-scatter. As shown in Fig. 1, and discussed in col. 7, lines 19 to 28 two different lasers are used, but are oriented to be collinear. Therefore, Applicants respectfully submit that Kramer fails to remedy the defects of Martin et al. and Hansen et al.

Accordingly, Applicants respectfully request that the rejection of claim 5 under 35 U.S.C. §103(a) be withdrawn.

The Examiner rejected claims 14 to 20 under 35 U.S.C. §103(a) as being unpatentable over Martin et al. (U.S. Patent No. 4,573,796) in view of Hansen et al. (U.S. Patent No. 4,284,412) and further in view of Hoffman (U.S. Patent No. 5,682,038). Applicants have canceled claims 14 and 15 without prejudice, but respectfully traverse this rejection as to remaining claims 16 to 20.

Claim 16 recites “dynamically assigning fluorescence detected in steps c) and f) to specific ones of the plurality of dyes depending on the excitation light sources.” Claim 17 recites “assigning any detected fluorescence to dyes known to be excited by the first excitation light source” and “assigning any detected fluorescence to dyes known to be excited by the second excitation light source.” Claim 19 recites “wherein the output of each integrator is dynamically assigned to one of the fluorescent labels depending on which laser is interrogating the particle.” Applicants respectfully submit that none of Martin et al., Hansen et al. or Hoffman, considered alone and in combination teach any of these limitations.

As explained on page 17, lines 1 to 24 of the specification, in an embodiment, the present invention uses a single fluorescence detector to detect fluorescence from both a first label excited by a first excitation light source and a different second label excited by a second excitation light source. The use of a single detector to detect fluorescence from multiple labels is advantageous, because it reduces expense and avoids the need for aligning additional detectors. However, to determine which label is fluorescing during a given time period, the excitation light source interrogating the particle during that time period must be identified. By using a separate scatter detector for each excitation light source, the particular excitation light source interrogating the particle for a given time period can be uniquely identified. The order of excitation light sources need not be known prior to usage of the system, because the order is revealed during use. Thus, integrated fluorescence is dynamically assigned to labels depending on which excitation light source is interrogating the particle at the time of integration.

Applicants respectfully submit that Martin et al., Hansen et al. and Hoffman fail to teach or suggest a system that is capable of dynamically assigning integrated fluorescence during use. All of Martin et al., Hansen et al. and Hoffman teach the use of separate fluorescence detectors for each label. Fluorescence detected by a given fluorescence detector can only correspond to a single label, thereby rendering (dynamic) assignment unnecessary.

Hansen et al. teach the use of a single detector for detecting a single dye that can be excited by two different lasers. However, this is not dynamic assignment, because the detector always detects emission light from the same dye. In contrast, the present invention, as claimed, uses a single detector to detect light from multiple dyes and detected light is dynamically assigned to one of the multiple dyes based on which excitation light scatter is detected at the time the emission light is detected. Accordingly, Applicants respectfully submit that claims 16, 17 and 19 are patentable over Martin et al., Hansen et al. and Hoffman, both alone and in combination.

Claim 18 depends from claim 17 and by definition contains all of the limitations of claim 17. Accordingly, Applicants respectfully submit that claim 18 is patentable over Martin et al., Hansen et al. and Hoffman for the reasons given above for claim 17 as well as because of the

additional limitations contained therein. In particular, claim 18 recites “wherein at least one of the plurality of fluorescence detectors comprises a filter that only passes light emitted by a first dye upon excitation by the first excitation light source and light emitted by a second dye upon excitation by the second excitation light source.” Applicants respectfully submit that Martin et al., Hansen et al. and Hoffman fail to teach or suggest the use of a multi-band pass filter and therefore fail to teach or suggest this limitation.

Additionally, as explained above, Martin et al. and Hansen et al. fail to teach or suggest a system consisting essentially of “a plurality of triggers, each of the plurality of triggers being connected to a separate one of the plurality of scatter detectors” as recited in claim 19. Applicants respectfully submit that Hoffman fails to remedy this defect of Martin et al. and Hansen et al. Hoffman is directed to a flow cytometry system that is excited by two lasers. However, the system does not have separate scatter sensors configured to detect light from each of the lasers. Accordingly, Applicants respectfully submit that claim 19 is patentable over Martin et al., Hansen et al. and Hoffman considered alone and in combination.

Claim 20 depends from claim 19 and by definition contains all of the limitations of claim 19. Applicants respectfully submit that claim 20 is patentable over Martin et al., Hansen et al. and Hoffman for the reasons given above for claim 19 as well as because of the additional limitations contained therein.

Accordingly, Applicants respectfully request that the rejection of remaining claims 16 to 20 under 35 U.S.C. §103(a) be withdrawn.

CONCLUSION

The Applicants believe that all pending claims are in condition for allowance and such action is earnestly requested. If the present amendments and remarks do not place the Application in condition for allowance, the Examiner is encouraged to contact the undersigned directly if there are any issues that can be resolved by telephone with the Applicants representative.

A fee of \$790 is believed due for the filing of a Request for Continued Examination with this Response and Amendment. The Commissioner is hereby authorized to charge payment of this fee and any other fees due with this communication to Deposit Account No. 19-2090.

Respectfully Submitted,

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Appendix A

Interview Summary

A telephonic interview was held on July 5, 2007 with Examiner Juan Valentin, one of the inventors, David Yang, and the Applicants' representative, Marc Karish. No exhibits or proposed amendment was submitted prior to the interview.

The Examiner, the inventor and the Applicants' representative discussed possible ways to potentially overcome the prior art rejection to claim 1 over Martin et al. by further limiting the scope of the claim. No agreement was reached.

The Examiner indicated that the rejection of claims 16 to 18 under 35 U.S.C. §101 would be withdrawn in the next Office action.

The inventor and the Applicants' representative discussed what is being claimed by the limitation of "dynamically assigning" in claim 16, pointing to the specification as originally filed (page 17, lines 14 to 24). The Examiner indicated that an argument specifically explaining what is being claimed by "dynamically assigning" with specific reference to the specification would aid the Examiner in determining whether Hoffman reads on the claim language. No agreement was reached.